Intraoperative pectoral nerve block (Pec) for breast cancer surgery: A randomized controlled trial

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Abstract

Background and Aims: In centers with high turnover of breast surgeries, pectoral nerve block (Pec II) is time-consuming and requires ultrasound familiarity for administration. We decided to block the same nerves under vision after resection to evaluate postoperative analgesic effects.
Material and Methods: Sixty patients scheduled for modified radical mastectomy were enrolled in this prospective, randomized, placebo-controlled, triple-blinded study. All patients received standardized general anesthesia. After surgical resection, infiltration of either ropivacaine (Group A) or saline (Group B) was given under vision at two points: 20 ml in the fascia over serratus anterior and 10 ml in the fascia between pectoralis major and minor at the level of the third rib. The primary outcomes measured were the time to first request for analgesia after extubation and total dose of analgesics needed, and secondary outcome included pain scores using the Numerical Rating Scale over 24 h. Analgesics used postoperatively were fentanyl citrate and paracetamol. We used Student's *t*-test to analyze quantity of analgesics needed, the nonparametric Mann–Whitney *U*-test for time to first request of analgesic, and Fisher's exact test for pain scores.
Results: No patient in Group A required fentanyl. The mean time to first request for analgesia and mean dose of paracetamol required was 353.93 ± 135.03 min and $2.71 \pm 0.462.71$ g in Group A and 27.17 ± 18.08 min and 3.53 ± 1.074 g in Group B [$P = 0.002$]. Significantly more patients in Group A had mild pain scores compared to Group B.
Conclusion: Pec II block with ropivacaine delivered under vision reduced analgesic requirement and pain scores significantly.

Keywords: Breast neoplasm, modified radical mastectomy, nerve block, postoperative pain, ropivacaine

Introduction

Perioperative analgesia for surgery in carcinoma breast utilizes significant quantities of opioids as compared to cosmetic breast surgeries. Ultrasound-guided modified pectoral nerve block (Pec) initially described for cosmetic breast surgeries provides excellent analgesia, but is resource-intensive in terms of trained manpower and equipment.[1] Opioids might alter oncological outcomes by changes in the tumor microenvironment.[2] Regional anesthesia reduces the need for perioperative opioids and thus may improve the outcome.[2] We decided to perform the Pec II block under vision after resection of tumor, without ultrasound and evaluated the postoperative analgesic and opioid sparing effects of the nerve block on patients undergoing modified radical mastectomy.

Material and Methods

This prospective, randomized, placebo-controlled, triple-blinded, parallel group, single-center trial was conducted from January to June 2016 after approval of the Institutional Review Board and Ethics Committee in our hospital. We

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included all American Society of Anesthesiologists (ASA) physical status I and II female patients between the ages of 18 and 70 years undergoing modified radical mastectomy for carcinoma breast after obtaining informed audio/video consent of participants. Patients with local anesthetic allergy, locally advanced breast malignancies with skin ulceration or infiltration of chest wall, bleeding dyscrasias, patients on anticoagulants, and deranged liver function tests were excluded from the study. All patients were taught how to define pain using the Numerical Rating Scale (NRS) 0–10; 0 = no pain, 1–3 = mild pain, 4–6 = moderate pain, and 7–10 = severe pain during the preoperative visit.[3]

After overnight fasting patients were premedicated with alprazolam 0.25 mg and ranitidine 150 mg orally the night before and 2 h before surgery. All patients received standardized general anesthesia with intravenous (IV) propofol for induction of general anesthesia, nitrous oxide – oxygen – sevoflurane for maintenance along with IV vecuronium for neuromuscular blockade. Supraglottic airway device I-gel was used to secure the airway. IV ondansetron was used as antiemetic and IV fentanyl citrate 2 µg/kg for analgesia intraoperatively. Any further rise in blood pressure or heart rate over 20% of baseline was treated by increasing the concentration of sevoflurane.

The drug used for the study was 0.2% ropivacaine, a local anesthetic agent, available as a 2 mg/ml solution in 20 ml ampoules in our institution for injection. The placebo solution, 0.9% sodium chloride, was taken from standard hospital supply. Study and placebo trial solutions were colorless, 30 ml in volume and were presented identically in 50 cc syringes. The patients were randomly allocated into two groups using computer-generated random numbers. The group allocation numbers were kept in a sealed envelope which was opened by investigator A (first author) after the patient was taken up for surgery. Investigator A prepared 30 ml of either 0.2% ropivacaine or 0.9% saline loaded into the 50 cc syringe under strict aseptic precautions according to the number in the envelope. Group A received 0.2% ropivacaine and Group B received 0.9% saline. Investigator A did not participate in subsequent clinical care or outcome assessment of the patients. The filled syringe was handed over to investigator B (second author) in the operation theatre who conducted the anesthesia for the patient. After completion of the surgery and wash of the area of dissection, investigator C (third author) injected 20 ml of the solution in the syringe beneath the pectoralis minor so as to infiltrate under the fascia, over serratus anterior [Figure 1] (Injection between Pectoralis Minor and fascia over Serratus Anterior) and 10 ml between the pectoralis major and pectoralis minor infiltrating under the fascia at the level of the third rib [Figure 2]. (Injection between Pectoralis Major and Pectoralis Minor) Then
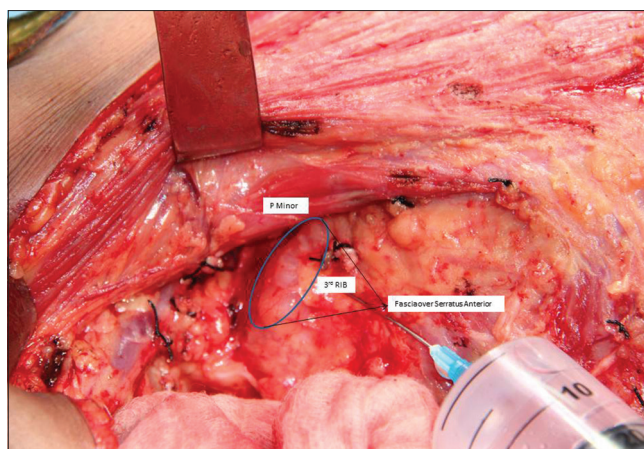

Figure 1: Injection between Pectoralis Major and Pectoralis Minor

wound was closed. Participants (patients) and investigating personnel (second and third authors) did not know whether the syringes contained ropivacaine or saline.

Postoperative analgesia regimen was standard in both groups. After reversal from anesthesia patients were extubated and shifted to the recovery room. When awake patients were asked to evaluate their pain intensity according to NRS scale by the second author. If it was more than 3 IV fentanyl citrate, 0.5 µg/kg was given for immediate pain relief and IV paracetamol 1 g infusion was started to go for more than 10 min. NRS was reassessed after 10 min. If NRS >3, 10 µg IV fentanyl citrate was given every 10 min till NRS became <3.

One hour after surgery, patient was shifted to postoperative ward for overnight monitoring and received IV pantoprazole and domperidone as per hospital protocol. Pain was assessed and treated according to NRS at rest and movement (pain on moving the ipsilateral arm) 1 hour (from the time patient woke up) after surgery and thereafter every 6 h for the next 24 h by investigator B. Analgesia was managed using IV paracetamol 1 g. If NRS was >3 after 10 min of infusion, 10 µg IV fentanyl citrate was given every 10 min till NRS became <3.

Fentanyl was given for immediate pain relief (rescue analgesic) and paracetamol for long duration pain relief, which is our hospital protocol for patients undergoing mastectomy without nerve blocks. We assumed that pain relief was inadequate and nerve block ineffective if patient complained of pain in immediate recovery period.

The primary outcome measures studied were: (a) duration of analgesia (time of the first rescue analgesia after extubation); (b) total cumulative dose of fentanyl and paracetamol needed for the first 24 h to maintain NRS <3. Secondary outcome measure analyzed was the number of patients with mild, moderate and severe postoperative pain (NRS). Any adverse

effects such as local anesthetic toxicity, hemodynamic instability, respiratory depression, paresthesia, pneumothorax, hematoma, re-explorations, or nausea and vomiting were recorded. Postoperative complications after 24 h were noted from the file.

The data were analyzed statistically using SPSS 11.0 (LEAD Technologies, Inc., Charlotte, North Carolina, USA) software. Based on the pilot study conducted with 10 patients (10 patients who were not included in the main study) in each group (mean duration of analgesia (SD): 406 ± 127.91 min and 25 ± 14.14 min for Group A and B, respectively), it was calculated by the statistician (fourth author) that a sample size of 30 patients in each group was required by fixing the level of significance at 0.05 and power at 80%. The statistician who conducted the analysis did not know which group had received the study drug. Student's *t*-test was used for normally distributed variables (age, intraoperative time, and total dose of paracetamol) and the corresponding nonparametric test, Mann–Whitney *U*-test for those continuous variables (time to first analgesic request) not following normality. The categorical variables (NRS at rest and NRS on movement) were tested using Fisher's exact test. The variables with *P* value <0.05 were considered to be statistically significant.

Results

During the study period, 63 patients fulfilled the inclusion criteria, out of which three patients declined to participate. Thirty patients were allocated in each group for the study. Two patients were excluded from the study as immediately after infiltration of solution leakage of infiltrate was noted from injection site before skin closure. These patients were observed for 24 h but not taken up for analysis. After analysis it was found that the two patients belonged to Group A. Hence, we had 28 patients in Group A and 30 patients in Group

B for final analysis. The two groups were comparable with respect to age, duration of surgery, and ASA status [Table 1].

The mean duration of analgesia was significantly longer in Group A than in Group B [Table 2]. Group A did not require any fentanyl. Group B required a mean fentanyl dose of 34.67 ± 13.58 μg. The mean dose of paracetamol required was significantly less in Group A than in Group B [Table 2] over 24 h. Significantly more patients had mild pain and fewer patients had moderate pain in Group A compared to Group B both at rest and on movement [Table 3], at all measured time points. No patient was lost to follow-up for the first 24 h (*n* = 58). None of the patients developed any adverse events such as local anesthetic toxicity, hemodynamic instability, respiratory depression, paresthesia, pneumothorax, hematoma, re-explorations, or nausea and vomiting. Wound infection was noted in three patients from records around 15–20 days postoperatively. One patient belonged to Group A and two patients to Group B. None of them required major interventions.

Discussion

Currently, an increase in usage of peripheral nerve blocks as a part of comprehensive anaesthesia care regimens is seen.[4] Even single-shot regional techniques seem to give excellent early analgesia.[5] Blocking the sensory supply to breast, axilla, and over the pectoral muscles provides adequate analgesia in the postoperative period. In our study the first injection of 20 ml below pectoralis minor so as to infiltrate the serratus anterior fascia and spread the injectate into the axilla at the level of third rib addressed the sensory supply of the breast, which is mainly derived from the branches of thoracic intercostal nerves T2–T5 and the axilla supplied
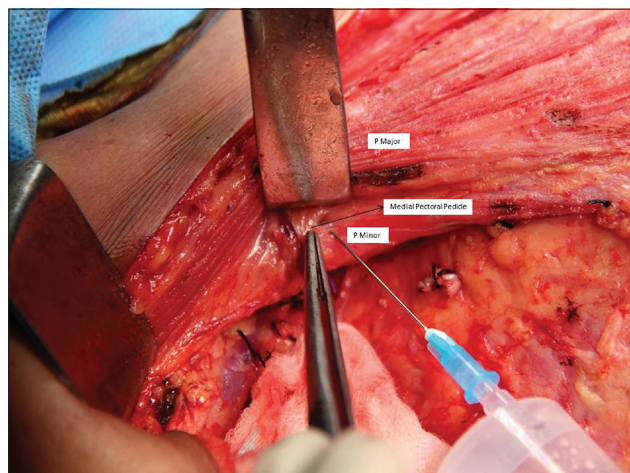

Figure 2: Injection between Pectoralis Minor and fascia over Serratus Anterior

Table 1: Demographic data

	Group A (*n*=28) mean±SD	Group B (*n*=30) mean±SD	*P*
Age	50.18±8.17	50.63±9.31	0.844
Duration of surgery	88.39±25.26	91.5±35.55	0.704
ASA 1	13	15	0.986
ASA 2	14	16	

Group A=Ropivacaine infiltration group. Group B=Saline Infiltration group.

Table 2: Comparison of analgesic usage between the two groups

	Group A (*n*=28) mean±SD	Group B (*n*=30) mean±SD	*P*
Time to first request for analgesia	353.93±135.03	27.17±18.08	0.002
Total paracetamol dose in g	2.71±0.46	3.53±1.074	0.002
Total fentanyl dose in μg	0.0	34.67±13.58	

Group A=Ropivacaine infiltration group. Group B=Saline infiltration group

Table 3: Number of patients with mild and moderate pain at rest and on movement at different time points

Time	Pain assessed at	Severity of pain	Group A (*n*=28)	Group B (*n*=30)	Total	*P*
1 h	Rest	Mild	27	19	46	0.003
		Moderate	1	11	12	
	Movement	Mild	26	11	37	<0.001
		Moderate	2	19	21	
6 h	Rest	Mild	28	21	49	<0.001
		<0.001 Moderate	0	9	9	
	Movement	Mild	25	10	35	0.001
		Moderate	3	20	23	
12 h	Rest	Mild	28	25	53	0.053
		Moderate	0	5	5	
	Movement	Mild	25	8	33	<0.001
		<0.001 Moderate	3	22	25	
18 h	Rest	Mild	28	21	49	0.002
		Moderate	0	9	9	
	Movement	Mild	24	10	34	<0.001
		<0.001 Moderate	4	20	24	
24 h	Rest	Mild	28	23	51	0.011
		Moderate	0	7	7	
	Movement	Mild	26	9	35	<0.001
		<0.001 Moderate	2	21	23	

Data presented as number of patients and analysed using Fisher's exact test. Group A=Ropivacaine infiltration group. Group B=Saline Infiltration group

by the long thoracic nerve and thoracodorsal nerve. The second injection of 10 ml between the pectoralis major and minor at the level of third rib blocked both the pectoral nerves supplying the fascia over the pectoralis major, which is removed during modified radical mastectomy adding to pain relief. The primary outcome of our study showed a statistically significant increase in the mean duration of analgesia and decrease in the cumulative analgesic requirement for the first 24 h in Group A. Pain scores assessed as secondary outcome showed that NRS at rest and movement were less in Group A. These results correlated with the hypothesis projected by the pilot study.

One of the strengths of this study was that it was a triple-blinded, randomized, placebo-controlled trial. Hence role for bias was minimal. To our knowledge this is one of the first studies to evaluate the analgesic effect on Pecs II block for patients undergoing modified radical mastectomy where multiple nerves supplying the area of dissection are addressed with only two injections given under vision. This technique did not require familiarity with ultrasound in operation theatres. In centers with time constraints due to high turnover, this technique is less time-consuming. Patient discomfort associated with breach of privacy of receiving a nerve block around the breast when awake is avoided. In patients, who were administered the preoperative Pec II block using an ultrasound, fluid-filled tissue planes were encountered during axillary tail dissection. Inability to use the electrocautery during surgical dissection was due to local anesthetic spread along the tissue planes.[6]

In the presence of tissue edema, tissue conductance increases, so causes lower resistance, resulting in reduced electrocautery efficacy.

In our study as the block was at the end of the surgery, it was safer and quicker (an extra time of 2 min on an average added to the operating time) with structures dissected out and easily identified, thus avoiding this complication.

An average of 8 h of postoperative analgesic duration was noted after ultrasound-guided Pec II block in patients who underwent cosmetic breast surgeries.[1] In our study the average postoperative analgesic duration was 6 hours with 7 out of 28 patients in the study group reporting postoperative pain relief for more than 8 h in spite of the fact that all patients underwent modified radical mastectomies – a potentially more destructive surgery. Statistically significant lower visual analog scale pain scores, postoperative morphine consumption were observed in patients who received Pecs II block with ultrasound preoperatively than in the control group patients who received general anesthesia alone for breast cancer surgery.[7] Mean time to first request of analgesia was 170 ± 11.2 min in the Pec group in their study as compared to 353.93 ± 135.03 min in our study. This reduced time is possibly due to the fact that the block was given preoperatively. This provided perioperative analgesia but reduced duration of postoperative analgesia. Moreover, as our block was given at the end of resection and after wash, the local anesthetic solution was more likely to be contained in the tissue plane in which it was deposited

than a preoperatively deposited solution that might leak out intraoperatively during tissue dissection.

We did not compare the effect of Pec block given under vision with ultrasound-guided block. Infiltration with 0.9% saline was used in the placebo group (Group B) to avoid bias in assessment and to assess if the volume of fluid over the nerve had any anesthetic effect. Patients in the Group B who had received saline instillation had an average of 27 min before first analgesic request which could be due to the pressure effect on the nerve, thus blocking nerve conduction and also due to dilution of the inflammatory mediators produced at surgical site, thus producing analgesia.[8]

In breast surgeries done under general anesthesia, opioids form the back bone of perioperative analgesia. Reducing the use of opioids in oncological surgeries may improve oncological outcomes as opioids have been reported to have immune modulatory effects in addition to their analgesic effect such as promotion of cell migration and expression of NET 1 gene.[9] None of the patients in the study group required rescue analgesic (fentanyl) in the recovery room or postoperative ward.

Nerve blocks for postoperative analgesia when given along with general anesthesia do not require a high concentration of local anesthesia. We used ropivacaine for this study due to its efficacy in control of postoperative pain and lower propensity for motor block.[10] The incidence of cardiotoxicity and central nervous system toxicity as a result of inadvertent intravascular injection of ropivacaine appears to be low.[11] Moreover, local anesthetic-based pain relief has been proposed to have cytotoxic effects on neoplastic cells by altering the tumor microenvironment and may prove to be doubly beneficial in terms of a pain-free perioperative period and also improved oncological outcomes.[12,13]

Nerve blocks under ultrasound guidance carry a risk of accidental nerve and vascular puncture.[14,15] Intravascular injection into the pectoral branch of the thoracoacromial artery is a possibility in preoperative ultrasound-guided blocks when needle traverses high in the axilla.[16] In our technique as the infiltration is done under vision after dissection and identification of the structures, these complications can be avoided. We did not notice any block-related complications such as bleeding or pneumothorax.

Tools for measuring postoperative pain are subjective. The sensory level of the block was not assessed. We have attempted to overcome this by using two additional measures: duration of analgesia (time to first request for analgesia) and total cumulative analgesic consumption. Another limitation of this

study was that opioid sparing effect of regional anesthesia could not be utilized perioperatively as block was given post breast resection. The analgesic effect of the nerve block on quality of night sleep was not assessed. Pec II block addresses the lateral branches of the thoracic intercostal nerves and so the anterior branches of the intercostal nerves supplying the internal mammary region could be spared. We did not perform the transversus thoracic muscle plane block, which could possibly further increase the quality of analgesia.[17] The effect of the regional infiltration on chronic pain was not studied, though studies with Pec blocks have shown that it reduces pain intensity for up to 7 days.[18] Persistent pain after breast cancer surgery is believed to be due to dysfunction of pectoral nerves. Further modifications like using bupivacaine or additives such as ketamine or dexmedetomidine to increase duration of analgesia could have been explored. Follow-up of patients for a longer time in the postoperative period could have been done to study the effect of our nerve block technique on post mastectomy pain syndrome.

Conclusion

Pec II block with ropivacaine delivered under vision reduced analgesic requirement and pain scores significantly. Detailed study of anatomy could reveal more such simple techniques for nerve blocks under vision for better postoperative pain relief in other surgeries.

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Nil.

Conflicts of interest
There are no conflicts of interest.

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